

Serial No. 09/701,132  
Attorney Docket No. 6433/80968

#### REMARKS

Continued prosecution and consideration of the claimed subject matter in the above-identified patent application is respectfully requested.

##### I. The Amendments

Claims 1-31 were cancelled previously. Claims 33, 36, 39, 43, 44, 45, 50, 51, 52, 53, 54, 55, 62, 64, and 65 are cancelled herein. Claims 35, 37, 40, 41, 46, 47, 48, 57, 58, 59, 60, 61, 63, 66, 67, and 68 have been amended herein. Claim 69 has been added. Claims 32, 34, 35, 37, 38, 40, 41, 42, 46, 47, 48, 49, 56, 57, 58, 59, 60, 61, 63, 66, 67, 68 and 69 are present in the case and are before the Examiner.

The claims have been amended along the lines helpfully suggested by the Examiner to maintain the claimed subject matter within the bounds of the restriction. Claim 37 has been amended to more specifically recite a useful primer. New claim 69 obtains its support in the specification at least from the disclosures of Table 3 wherein the primers used for obtaining the nucleic acid of the H11 flagellin gene sequence were from the recited region of SEQ ID NO:13. It is thus seen that no new matter has been presented through the requested amendments.

##### II. Title of the Invention

The title previously was objected to for being insufficiently descriptive of the invention. The title was amended in a previous Reply to "Sequences for the Detection of *Escherichia coli*". It is believed that that amendment overcame

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the objection to the original title as mentioned in the previous Reply.

### III. The Rejections

#### A. Rejections under 35 U.S.C. § 112, 1<sup>st</sup> Paragraph

Claims 32-68 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to provide enablement for any nucleic acid comprising SEQ ID NO: 13, 56, or 57 or comprising a part of SEQ ID NO: 13, 56, or 57.

The present amendment cancels claims 33, 36, 39, 43, 44, 45, 50, 51, 52, 53, 54, 55, 62, 64, and 65, and presents newly amended claims directed toward a subset of the earlier subject matter in the interests of speeding prosecution and obtaining claims of specific interest to the present inventors. We reserve the future right to prosecute in a continuing patent application the subject matter no longer being prosecuted as a result of the present amendment.

It is believed that the newly amended claims obviate this basis for rejection as the former claim language directed to "a part thereof" has been removed. It is submitted there is support for additional bases on either side of the enumerated sequence. The sequence from position 586 to position 810 is in a central portion of SEQ ID NO: 13, and the sequence from 586 to 810 is therefore flanked by additional nucleotides in SEQ ID NO: 13.

In addition, paragraph [00162] of the specification describes amplification of the H35 type strain using the primers from position 586 to 606 and 791 to 810 of SEQ ID NO: 13. The

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resulting fragment comprises the sequence from position 586 to 810, and in addition has an insertion sequence. Accordingly, it is submitted that the specification provides support for not only additional sequences on the ends of the sequence from position 586 to position 810 of SEQ ID NO: 13, but also for additional sequence in a central portion of the sequence of SEQ ID NO: 13.

In addition, the specification discloses at paragraph [00113] that the flagellin gene for H11 is cloned in plasmids with a trc promoter, and SD sequence. Moreover, at paragraph [00135] and Table 3A, the specification indicates that plasmid pPR1981 encodes the H11 flagellin, clearly indicating that the flagellin gene is contained within plasmid sequence.

Table 3A also indicates that primers 1868 and 1870 were used to amplify the H antigen gene. Cloning primer Table 3B indicates that cloning primer 1868 contains an NcoI site, and cloning primer 1870 contains a BamHI site. Accordingly, it is submitted that the specification clearly teaches that SEQ ID NO: 13 can have additional sequence at its ends.

It is further submitted that the Action has not carried its burden of showing a lack of enablement. More specifically, particularly for claims 32, 37 and 69, it is submitted that the claimed subject matter is well enabled as discussed above and the results obtained and disclosed in the specification. In view of this amendment, it is respectfully requested that the rejection of the claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

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It is noted that no evidence has been presented that shows that a skilled worker could not make and use a claimed nucleic acid. It is agreed that a few sequences have been disclosed that include nucleotides in addition to those from a recited region of SEQ ID NO:13. However, it must be remembered that this application was first filed in 2000, long after the wave of genetic engineering brought in by Cohen and Boyer and others washed in a new order in biological sciences. Workers of ordinary skill knew almost 20 years later in 2000 how to make and use DNA and nucleic acid primers. The Nobel Prize was given to Kary Mullis for PCR in 1993. As the Court in *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 at 91 (Fed. Cir. 1986) noted: "a patent need not teach, and preferably omits what is well known in the art." (Citation omitted.) It is thus submitted that the application has provided all of the enablement required for a worker of ordinary skill.

Furthermore, no evidence or argument has been provided to show that a nucleotide sequence containing the recited sequence would not work for a disclosed purpose. The Court in *In re Marzocchi & Horton*, 169 USPQ 367, 369-370 (CCPA 1971) ruled upon the propriety of a similar rejection in a chemical application. The Court held that the

"only relevant concern of the Patent Office under these circumstances should be over the truth of any such assertion [of efficacy]."  
[169 USPQ at 369; emphasis in the original.]

The Court went on to hold:

"it is incumbent upon the Patent Office, whenever a rejection on this basis [doubt as to enablement] is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate statement." (Emphasis in the original.)

The Marzocchi requirement of an explanation of "why" truth or accuracy of the disclosure is doubted has not been complied with. This rejection should therefore be withdrawn.

B. Rejections under 35 U.S.C. § 112, 2<sup>nd</sup> Paragraph  
Claims 33, 36-57, 60-64 and 66 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 39, 48, 52, 60 and 61 stand rejected as indefinite over the Table that lists the primers. The present amendment avoids this ground of rejection by reciting that the primers are of particular and certain nucleotides of SEQ ID NO:2.

Claims 33 and 36 were rejected over the term "are from about 10 to 20 nucleotides in length" but are now cancelled. A similar phrase with a different context has been added to claim 37.

Claims 37-39, 57 and 66 were rejected as allegedly being indefinite over the recitation of the term "corresponding"

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within the claims. Claim 39 has been cancelled and the term "corresponding" has been deleted from claims 37, 38, 57, and 66.

Claims 37-39, 41, 44, 45, 47-49, 56, 57, 62, 63, and 66 were rejected as allegedly being indefinite over the recitation of the term "a nucleotide sequence" within the claims. Although it cannot be agreed that that usage was at all indefinite, claims 39, 44, 45, 47, and 62, have been cancelled and the remaining amended claims refer to primers that comprise the full-length sequence to speed prosecution.

Claims 40-56, and 62-65 were rejected as allegedly being indefinite as to how the method steps accomplish the objective set for the in the claim. The amended claims now clarify how the detection of the presence of a particular H serotype of *E. coli* is accomplished by selective hybridization.

Claims 43, 44, 50, 51, 52, 55, and 62-65 were rejected in light of the recitation "a pair of nucleic acid molecules according to claim 32". Claims 43, 44, 50, 51, 52, 55, 62, 64, and 65 have been cancelled. Claim 63 does not contain this phrase, therefore has not been amended and should not be objected to on this basis.

Claims 52, 54 and 65 rejected as indefinite have been cancelled to speed prosecution.

Claim 60 was rejected over the recitation of "the composition of b". The claim has been amended to improve this language as well as in the similar claim 61 which recites the "composition of a".

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In view of the present amendments, it is respectfully requested that this ground for rejection of the pending claims under 35 U.S.C. § 112, second paragraph, be withdrawn.

3. Rejections under 35 U.S.C. § 102(b)

Claims 32-39 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Fields (*Journal of Clinical Microbiology*, 35:1066-1070 (May 1997)), teaching PCR amplification of the fliC gene of various H serotypes of *E. coli*, e.g. H5, H29, H56, H36, H53, H51 and H44.

However, as stated by the Examiner, the H serotypes set forth by Fields contain the nucleic acids of SEQ ID NOs: 7, 28, 50, and 54, whereas the presently amended claims do not contain those sequences. Therefore, presently there is no basis for this rejection.

Claims 32-39 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Ratiner (*Journal of Bacteriology*, 180:979-984 (Feb. 1998)), teaching *E. coli* flagellin FlA and flmA genes from serotypes H44, H54 and H55. The present claims specifically recite the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:13, 56, or 57. It is therefore submitted that a claimed sequence is not taught or suggested by the relied-upon art.

In view of the present amendment, it is respectfully requested that these grounds for rejection of the pending claims under 35 U.S.C. § 102(b) be withdrawn.

4. Rejections under 35 U.S.C. § 103(a)

Claims 57, 67, and 68 were rejected under 35 U.S.C. § 103(a) over the disclosures of Fields (*Journal of Clinical Microbiology*, 35:1066-1070 (May 1997)) in view of Ahren (*The Scientist*, 19(155):20-24 (July 1995)). The present claims specifically recite the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOs: 13, 56, or 57. It is therefore submitted that the claimed sequence is not taught or suggested by the relied-upon art, and that this basis for rejection should be withdrawn.

Claims 57, 67, and 68 were rejected as obvious over the disclosures of Ratiner (*Journal of Bacteriology*, 180:979-984 (Feb. 1998)) in view of Ahren (*The Scientist*, 19(155):20-24 (July 1995)). The present claims specifically recite the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOs: 13, 56, or 57. It is therefore further submitted that the claimed sequence is not taught or suggested by the relied-upon art, and that this basis for rejection should be withdrawn.

Claims 58-61, and 66 were rejected as allegedly obvious over the disclosures of Fields [*Journal of Clinical Microbiology*, 35:1066-1070 (May 1997)] in view of Ahren [*The Scientist*, 19(155):20-24 (July 1995)] and further in view of Stevenson [*Journal of Bacteriology*, 176:4144-4156 (1994)]. The present claims specifically recite the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOs: 13, 56, or 57. It is therefore again submitted that the claimed sequence is not taught or suggested by the relied-upon art, and that this basis for rejection should be withdrawn.



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#### IV. NEW ART

Also enclosed herewith is a copy of the European Search Report for the EPO version of this application and an article cited therein that was not already of record here. That enclosed article is Gannon et al. (Mar. 1997) *J. Clin. Microbiol.*, 35:656-662. A Form PTO-1149 citing that article is also enclosed. The remaining art cited in that search is of record here. It is noted that the EPO Search Report is dated March 3, 2005, a date less than three months ago. It is therefore believed that no formal statement is needed as to knowledge of the Search and its contents.

#### V. SUMMARY

Claims 1-31 were cancelled previously. Claims 33, 36, 39, 43, 44, 45, 50, 51, 52, 53, 54, 55, 62, 64, and 65 are cancelled herein. Claims 35, 37, 40, 41, 46, 47, 48, 57, 58, 59, 60, 61, 63, 66, 67, and 68 have been amended herein, and claim 69 has been added. Each basis for rejection has been dealt with and overcome or otherwise made moot.

It is therefore believed that this application is in condition for allowance of all of the pending claims. An early notice to that effect is earnestly solicited.


Our check No. 093764 in the amount of \$100.00 to cover the cost of newly added independent claim 69 that is also a claim in excess of twenty claims is enclosed herewith. No further fee or petition is believed to be necessary. However, should any further fee or petition be needed, please charge our

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Deposit Account No. 23-0920, and deem this paper to be the required petition.

The Examiner is requested to phone the undersigned should any questions arise that can be dealt with over the phone to expedite this prosecution.

Respectfully submitted,

By   
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Enclosures


Petition and Fee  
EPO Search Report and art  
Form PTO-1149  
Added claim fee

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CERTIFICATE OF MAILING

I hereby certify that this Reply, its enumerated attachments, Petition for Extension of time and its fee and added claims fee are being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: MAIL STOP AMENDMENT, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on May 27, 2005.

By   
Edward P. Gamson



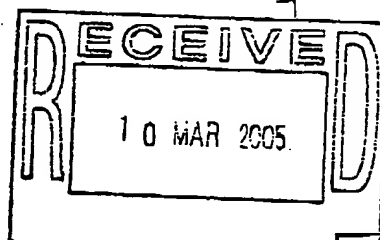
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Anmeldung Nr./Application No./Demande n°//Patent Nr./Patent No./Brevet n°

99923309.1-1212/AU9900385

Anmelder/Applicant/Demandeur/Patentinhaber/Proprietor/Titulaire  
THE UNIVERSITY OF SYDNEY

## COMMUNICATION

The European Patent Office herewith transmits the partial European search report under Rule 46(1) EPC relating to the above-mentioned European patent application.

Copies of the documents cited in the search report are enclosed.

The applicant's attention is drawn to the following:

The search Division informs the applicant that if the European search report is also to cover inventions other than the invention first mentioned in the claims, a further search fee must be paid for each of these inventions, within ONE MONTH after notification of this communication.

If the application has been filed up to 30 June 1999, the search fee in force before 01 July 1999 (EUR 869.--) or the equivalent applicable on the date of payment is payable.

This applies also to the search fees requested under Rule 46(1) EPC.

See also OJ EPO 06/1999, 405.

- ☐ The abstract was modified by the Search Division and the definitive text is attached to the present communication.
- ☐ Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

Ms. G. LLORE

9.10.2005



## Note to users of the automatic debiting procedure:

Unless the EPO receives prior instructions to the contrary, the search fee(s) will be debited on the last day of the period for payment. For further details see the Arrangements for the automatic debiting procedure, Supplement to OJ EPO 02/1999.

REGISTERED LETTER



European Patent  
Office

**SUPPLEMENTARY  
PARTIAL EUROPEAN SEARCH REPORT**

Application Number

under Rule 46, paragraph 1 of the European Patent Convention  
EP 99 92 3309

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages.	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cls.)
X, D	SCHOENHALS G ET AL: "COMPARATIVE ANALYSIS OF FLAGELLIN SEQUENCES FROM ESCHERICHIA COLI STRAINS POSSESSING SEROLOGICALLY DISTINCT FLAGELLAR FILAMENTS WITH A SHARED COMPLEX SURFACE PATTERN" JOURNAL OF BACTERIOLOGY, WASHINGTON, DC, US, vol. 175, no. 17, September 1993 (1993-09), pages 5395-5402, XP000974655 ISSN: 0021-9193 * the whole document *	1-5, 7-10, 19, 21-25	C12Q1/10 C12Q1/68 C12R1/19
X	GANNON V P J ET AL: "USE OF THE FLAGELLAR H7 GENE AS A TARGET IN MULTIPLEX PCR ASSAYS AND IMPROVED SPECIFICITY IN IDENTIFICATION OF ENTEROHEMORRHAGIC ESCHERICHIA COLI STRAINS" JOURNAL OF CLINICAL MICROBIOLOGY, WASHINGTON, DC, US, vol. 35, no. 3, May 1997 (1997-05), pages 656-662, XP000957649 ISSN: 0095-1137 * the whole document *	1-5, 7-10, 19, 21-25	TECHNICAL FIELDS SEARCHED (Int.Cls.)  C12N C12Q
-/-			
<b>LACK OF UNITY OF INVENTION</b>			
The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:			
see sheet B			
The present partial European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims.			
Place of search <b>The Hague</b>		Date of completion of the search <b>18 February 2005</b>	Examiner <b>Kools, P</b>
<b>CATEGORY OF CITED DOCUMENTS</b>		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons  & : member of the same patent family, corresponding document	
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document			

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EPO FORM 1503 03.02 (P04C53)



European Patent  
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# **SUPPLEMENTARY PARTIAL EUROPEAN SEARCH REPORT**

Application Number  
**EP 99 92 3309**

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cls)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X,D	RATNER YULI A: "New flagellin-specifying genes in some Escherichia coli strains" JOURNAL OF BACTERIOLOGY, vol. 180, no. 4, February 1998 (1998-02), pages 979-984, XP002318316 ISSN: 0021-9193 * abstract *	1	
P,X	REID S D ET AL: "SEQUENCE DIVERSITY OF FLAGELLIN (FLIC) ALLELES IN PATHOGENIC ESCHERICHIA COLI" JOURNAL OF BACTERIOLOGY, WASHINGTON, DC, US, vol. 181, no. 1, January 1999 (1999-01), pages 153-160, XP000978074 ISSN: 0021-9193 * the whole document *	1-5, 7-10, 19, 21-25	TECHNICAL FIELDS SEARCHED (Int.Cls)



European Patent  
Office

# LACK OF UNITY OF INVENTION SHEET B

Application Number  
EP 99 92 3309

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

**Inventions 1-64: claims 1-5, 7-10, 19, 21-25 (all partial)**

A nucleic acid molecule encoding all or part of an E. coli flagellin protein, having Seq ID No 1 (or other chosen from the sequences indicated below). Methods of detecting the H serotype of E. coli using said polynucleotide either alone or in combination with other genes, specified by sequence positions in figure 5 and 6. Kits for identifying said serotype using the specified nucleic acids.  
This group of inventions comprises 64 different sequences (Seq ID 1-8, 10-54, 56, 58-64, 66-68.).

**Inventions 65-68: claims 1-5, 7-10, 19-25 (all partial)**

This group of inventions is identical to the above except that it comprises 4 different sequences (Seq IDs 9, 55, 57 and 65), which are specified in claim 20.

**Inventions 69-79: claims 11-18, 21, 23-25 (all partial)**

Method of detecting the H and O serotype of E. coli using a nucleic acid derived from genes specified by sequence position in Figure 5 and 6. Kits for identifying said serotype using the specified nucleic acids.

**Inventions 79-169: claim 6 (partial)**

Primers of table 3, specifically recognizing polynucleotides encoding E. coli flagellin genes.  
This group of inventions comprises 90 different primer sequences.

## REASONS FOR THE LACK OF UNITY OF THE PRESENT APPLICATION

Nucleic acids sequences encoding the Escherichia coli fliC protein, specific primers and its use to identify serotypes is already known from the prior art. See for example Gannon et al. (1997), Schoenhals and Whitfield (1993). Therefore, the unifying concept of the present application is known from the prior art. In the light of the prior art, the problem and corresponding solutions of the present application can be defined as follows:

### Problem:

(A) The provision of further E. coli fliC encoding nucleotide sequences or parts thereof for the identification of the H serotype.



European Patent  
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**LACK OF UNITY OF INVENTION**  
**SHEET B**

Application Number

EP 99 92 3309

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

(A) (Solution 1: The nucleotide sequence corresponding to Seq ID No 1.  
Solutions 2-68: The nucleotide sequences corresponding to Seq IDs No 2-68  
Solutions 69-158: The nucleotides (primers) as outlined in table 3.

(B) (A second problem is formulated (for claims 11-18, 21, 23-25 (all partial), problem: The provision of further E.coli sequences useful for the identification of H and O serotypes.

Solutions 159-168 : The nucleotide sequences corresponding to those specified in claim 12 as outlined in figures 5 and 6.

In view of the fact that E.coli fliC nucleotide sequences have been disclosed in the prior art; due to the essential differences in the primary structure of the nucleotide sequences of the different

solutions, and due to the fact that no other technical features can be distinguished which, in the light of the prior art, could be regarded

as special technical features, the European search examiner is of the opinion that there is no single inventive concept underlying the plurality of claimed inventions of the current application within the sense of Article 82 EPC.

Thus only the first invention, i.e. claims 1-5, 7-10, 19, 21-25 (all partially) have been searched.

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